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CLINICAL ADVISORY

Revised, November 5, 2001

Inhalational Anthrax

Anthrax, caused by infection with the aerobic, spore-forming bacterium, *Bacillus anthracis*, occurs in three major syndromes: cutaneous, gastrointestinal and inhalational. Cutaneous anthrax requires the introduction of *B. anthracis* into the skin. Gastrointestinal (or oropharyngeal) anthrax results from ingesting *B. anthracis* spores, usually in meat from animals infected with anthrax. Inhalational anthrax requires the deposition of anthrax spores in the alveoli. Inhalational and gastrointestinal anthrax are the more severe forms of infection. Inhalational anthrax has been a very rare disease in the United States, with the first cases since 1978 occurring in 2001 following intentional release of spores.

Inhalational anthrax results from the deposition of spore-bearing particles of a size 1-5 microns in the alveolar spaces. It has been estimated that it takes 8,000 to 10,000 inhaled spores to cause infection in half of those exposed, but fewer spores may cause disease in a smaller proportion of those exposed, especially those who may be more susceptible for reasons that have not been adequately defined. Once in the alveoli, the spores are ingested by macrophages. If the macrophages cannot destroy all of the spores presented, then viable spores are transported to mediastinal lymph nodes. Germination of these spores may occur at any point up to 60 days after exposure. Disease rapidly follows germination of spores.

Inhalational anthrax is not characterized by pneumonia or bronchopneumonia, but rather by hemorrhagic lymphadenitis and hemorrhagic mediastinitis. Clinical findings are fever, chills, malaise, fatigue, shortness of breath, chest tightness or pain, cough (usually non-productive), abdominal pain and vomiting, lasting a few hours or days. This may be followed by a brief period of improvement, but then fulminant disease with fever, dyspnea, diaphoresis and shock. The course is further complicated by the frequent occurrence of hemorrhagic meningitis. Shock and cyanosis lead rapidly to death. There is little experience with the treatment of inhalational anthrax with antibiotics and intensive care, so the expected mortality in the contemporary medical setting is unknown. Among ten cases that have occurred thus far this year in the U.S., four persons have died and two have been discharged from the hospital.

Clinical indicators of inhalational anthrax are severe respiratory and systemic signs and symptoms with mediastinal widening and/or pleural effusion(s) on chest x-ray and limited evidence of pulmonary infiltrates. If chest x-ray is negative, a CT scan of the chest may reveal mediastinal lymphadenopathy, paratracheal fullness and hilar adenopathy. Patients may have respiratory stridor related to mediastinal widening and mass effect of lymphadenitis. Early in the course, the white blood count may not be elevated, but there may be bands on the differential count. Anthrax should be suspected with these clinical findings and in any patient with a history of known or possible exposure, or an occupation where exposure might have occurred.

Treatment of inhalational anthrax should be started promptly with ciprofloxacin, 400 mg, IV, every 12 hours or doxycycline, 100 mg, IV every 12 hours. *B. anthracis* is typically susceptible to multiple antimicrobial agents, but not extended-spectrum cephalosporins. Currently, it is recommended that patients with inhalational anthrax be treated with at least two agents to which the clinical isolate is known or presumed to be susceptible. Treatment with ciprofloxacin or doxycycline is continued for 60 days to cover spores that might germinate later. Although recent isolates of *B. anthracis* have tested susceptible to penicillin, there are indications that these organisms may produce penicillinases and therefore render penicillins less effective. Therefore, it is recommended that penicillins not be used alone for the treatment of inhalational anthrax.

Suspect inhalational anthrax in any individual with a history of exposure or occupational/environmental risk with a 2-5 day illness, with some or all of the following signs and symptoms: fever, sweats, headache, myalgias, fatigue, malaise, cough (usually non-productive), shortness of breath, chest discomfort, pleuritic pain, nausea, vomiting, diarrhea and abdominal pain. Obtain a white blood count, blood cultures and chest x-ray. If chest x-ray is normal or equivocal, obtain a chest CT. Rapid influenza tests can be done, but the patient and clinician should interpret a negative result in light of the fact that most influenza-like illness, even at times of circulating influenza virus, is not due to influenza virus, but to other respiratory viruses. If WBC, and chest x-ray and/or CT scan are abnormal or the patient is moderately or severely ill, then begin antimicrobial therapy. CSF should be obtained if meningeal signs are present and pleural fluid, if present, should be tapped for Gram stain and culture. If WBC and chest x-ray (or CT scan, if obtained) are normal, then observe closely pending blood cultures and initiate or continue prophylaxis. Acute and convalescent serology may be useful in confirming diagnosis in patients who have recovered. If the patient is asymptomatic or has symptoms, not in any way suggestive of inhalational anthrax, then begin antimicrobial prophylaxis, if exposure to anthrax spores is confirmed.

Report all suspected inhalational, cutaneous, septicemic, meningeal and gastrointestinal anthrax cases immediately to the health department (in Boston, Boston Public Health Commission at 617-534-5611) or to the Massachusetts Department of Public Health (617-983-6800).

For more information, see http://www.state.ma.us/dph/topics/bioterrorism/BT.htm, http://jama.ama-assn.org/issues/v281n18/ffull/jst80027.html and http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5043a1.htm. The MDPH information line on emergency preparedness and response is **1-866-627-7968**.